

COMPARISON OF REGIONAL AND GENERAL ANESTHESIA IN OBSTETRICS

WITH SPECIAL REFERENCE TO TRANSMISSION OF CYCLOPROPANE ACROSS THE PLACENTA

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During the past eight years, cyclopropane has been found to have many advantages as an obstetric anesthetic agent at the Sloane Hospital for Women. The speed of induction, the quick controllability of depth of anesthesia, and the possibility of ample oxygenation at all times has lead to preference for this agent. In only rare instances cyclopropane has been unsuccessful in relaxing a very tight uterus, which was accomplished by use of chloroform.

On the other hand, Smith¹ suggested a harmful effect of cyclopropane on the infant and Bundesen and co-workers² noted an infant death rate following use of this gas three times as high as with any other agent used for obstetric anesthesia. Roven-
tine and co-workers³ found that deep levels of anesthesia induced by cyclopropane in the mother were accompanied by decreased oxygenation of the infant and suggested using the lightest planes of anesthesia.

In view of these discrepancies of attitudes we felt obliged to examine the matter more closely. Regional and general anesthesia were studied clinically during various obstetric situations.

Clinical Data

Four obstetric situations were chosen for review: near-term elective cesarean section, premature vaginal vertex delivery, premature and term breech deliveries, and full-term vaginal vertex delivery.

Elective Cesarean Section.—Cases of elective cesarean section with patients under regional anesthesia, unsupplemented before the birth of the infant, were compared with those with patients under general anesthesia, in this case with cyclopropane. No patients in whom thiopental (Pentothal) induction was used, or to whom a relaxant was given, are included. All the patients were undergoing secondary or tertiary section, or had absolute cephalopelvic disproportion. None was in labor, and none had complications such as toxemia or placenta previa. All patients from 1952 through 1955 who satisfied the above requirements were included. During these four years, there was a change in

General anesthesia was compared with regional anesthesia as to its effects on mother and fetus in 2,856 vaginal deliveries at term. General anesthesia was used in 2,019 cases, and in 1,022 of these the anesthetic was cyclopropane. Biochemical data were obtained from maternal and fetal blood. In addition, three methods of evaluating the condition of the infant at birth were employed, including a special score based on certain cardiorespiratory and neuromuscular observations. The blood of most infants delivered of mothers receiving cyclopropane contained this gas in demonstrable amounts, but there was no obvious correlation between its concentration and the score noted for the infant. The gas probably induced a mild, readily reversible central narcosis. There was no biochemical evidence that it depressed placental function, but infants born with the mother under general anesthesia, specifically cyclopropane, were more depressed than those born with the mother under regional anesthesia.

anesthetic practice, with the trend to increasing the use of spinal anesthesia. Only two patients for whom elective sections were done were anesthetized with cyclopropane in 1955. We were unable to examine a group for whom emergency sections had been done, since spinal anesthesia was rarely chosen, either because of the need for great haste or because of hypovolemia from hemorrhage.

Premature Vaginal Vertex Delivery.—Premature vaginal vertex deliveries, in this clinic, are accompanied by the highest neonatal death rate and thus were chosen for study. Infants under 1,000 Gm. (2.2 lb.) were omitted because of a death rate of 95% irrespective of the anesthetic agent or method. Infants over 2,000 Gm. (4.4 lb.) were so similar to full-term infants in their postnatal behavior and survival that they also were omitted. The weights of the 130 infants in the group chosen for study therefore were from 1,000 to 1,999 Gm.

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Breech Deliveries.—In this clinic 35% of breech deliveries occur prematurely. It is of interest that 90% of the deaths occurring in infants after breech delivery are in this premature group. Cases of version and breech extraction are omitted from these figures because of the need of deeper anesthesia and a relaxed uterus.

TABLE 1.—Distribution of General Anesthetic Agents in Term Vaginal Vertex Deliveries

Anesthetic Agent	Vaginal Vertex Deliveries	
	No.	%
Nitrous oxide	916	45.3
Cyclopropane	1,022	50.7
Ethylene	54	2.7
Trichloroethylene	11	0.5
Ether	10	0.5
Chloroform	6	0.3
Total	2,019	100.

As a group for comparison, 2,856 patients who delivered vaginally at term (infants weighing over 2,500 Gm. [5.5 lb.]) during the year 1955, were chosen if they had been anesthetized by a purely regional, or general, method. In 837 cases in which regional anesthesia was used, 10.3% of patients received pudendal block or local infiltration of the episiotomy area, 44.4% received sacral or lumbar epidural block, and 43.0% received spinal anesthesia. The distribution of the 2,019 cases by general anesthetic agents used appears in table 1.

In summary, the cases omitted from this analysis are emergency cesarean sections, version and breech extraction, and premature deliveries of infants under 1,000 and over 2,000 Gm. In addition to these omissions, there may be a bias in the selection of cases. Cyclopropane is more likely to be used for delivery in cases of fetal distress and in other obstetric complications, while regional anesthesia is used when labor is well established and the pelvis is adequate.

TABLE 2.—Evaluation of Newborn Infant*

Sign	0	1	2
Heart rate	Absent	Slow (below 100)	Over 100
Respiratory effort	Absent	Slow Irregular	Good Crying
Muscle tone	Limp	Some flexion of extremities	Active motion
Response to catheter in nostril (tested after oropharynx is clear)	No response	Grimace	Cough or sneeze
Color	Blue Pale	Body pink Extremities blue	Completely pink

* Method of scoring: 60 seconds after complete birth of infant (disregarding cord and placenta), these five objective signs are evaluated and each given a score of 0, 1, or 2. A score of 10 indicates an infant in the best possible condition.

Three methods of comparison were employed: neonatal (28 days) death rates, scores at birth⁴ (table 2), and time to sustained respiration.

With use of neonatal death rates as a criterion, there was no significant difference in any of the four groups between those receiving regional or general anesthesia (table 3).

As an aid to evaluating the condition of an infant in the first few minutes after birth, a scoring system was devised and first used in 1952⁴ (table 2). After experience with over 16,000 scores, based on correlation with mortality, a division was made between those infants receiving scores of 0 to 4 and those of 5 to 10. Those with the lower scores are considered to be potentially sick infants, while those with scores of 5 or higher have a distinctly better prognosis. Examination of the death rates at each score shows a drop from 3.0% death rate at a score of 4 to 1.5% at score 5 (fig. 1). It is true that there is another abrupt drop between score 6 and 7, so that this

TABLE 3.—Comparison of Neonatal Death Rates with Type of Anesthesia

Type of Anesthesia	Elective Cesarean Sections			Premature Vaginal Vertex Deliveries			Breech Deliveries			Vaginal Vertex Full-term Deliveries		
	No.	NND*	%	No.	NND	%	No.	NND	%	No.	NND	%
Regional	166	1	0.6	78	11	14.1	98	8	8.17	837	3	.36
General	67	1	1.5	52	5	9.6	284	23	8.10	2,019	5	.25

* NND = neonatal death rate.

division might be used. Recalculating the data in some groups on the basis of including groups 5 and 6 did not result in any change of significance in the groups examined. As will be noted in table 4 and figure 2, the scores of infants in the premature vaginal vertex and breech groups were not significantly different whether the anesthesia was general or regional. However, the scores of full-term infants were significantly better by the chi square test

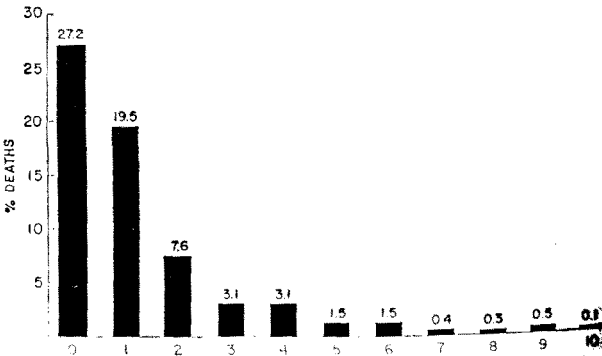


Fig. 1.—Distribution by score of 97 deaths in 6,666 infants from the Sloane Hospital for Women.

($p < 0.001$) in both vaginal vertex and elective cesarean section groups, if regional anesthesia was used.

Since 1954, another method of evaluation has been routinely charted. This observation has been termed "time to sustained respiration." Our attempt to use "crying time" and "breathing time" failed to yield useful correlations with morbidity or mortality. The time elapsed until the infant sustains spontaneous respiration is recorded in seconds, after delivery of the entire infant. There were insufficient data in the elective cesarean sections and premature

vaginal vertex deliveries for comparison of regional and general anesthetic methods. No significant effect of anesthetic technique was observed in relation to

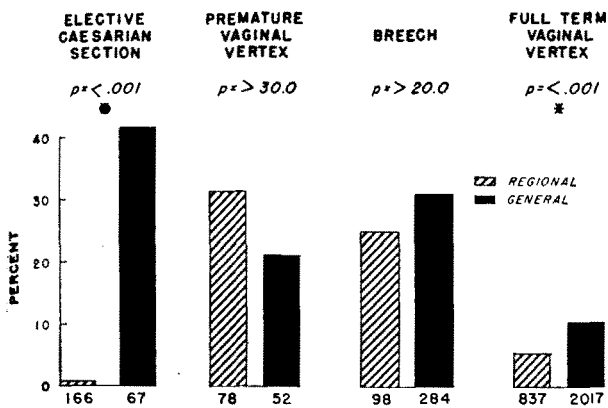


Fig. 2.—Regional versus general anesthesia, scores 0-4.

breech deliveries (table 5 and fig. 3 and 4). However, the incidence of delayed onset of sustained respiration following full-term vaginal vertex de-

after absorption of carbon dioxide and oxygen (method as applied to Kopp-Natelson microgasometer to be published⁶). Factors for conversion of manometric pressure differences to volume per cent of cyclopropane were calculated for the micromanometric method using the equation of Van Slyke and Neill.⁷ The factors for solubility and rate of reabsorption were from Orcutt and Waters.⁸

Because this method does not allow for distinction between the contributions of nitrogen and cyclopropane to the pressure of the residual gas, experiments were performed on mothers who were breathing air. Fifteen blood specimens of five mothers and their infants were analyzed for residual nitrogen. The average nitrogen content of the specimens of maternal and umbilical cord blood of these patients was 1.2 vol. % (table 7), which is in agreement with Van Slyke and Neill.⁷

Because of the intermittent need for pain relief and because of the indeterminate duration of the second stage of labor, the degree of nitrogen "wash-out" from the blood and the amount of cyclopropane administered was variable. A study of the rate of

TABLE 4.—Comparison of Scores with Type of Anesthesia

Scores Type of Anesthesia	Elective Cesarean Sections*						Premature Vaginal Vertex Deliveries						Breech Deliveries						Vaginal Vertex Full-term Deliveries†					
	Score of 0-4			Score of 5-10			Score of 0-4			Score of 5-10			Score of 0-4			Score of 5-10			Score of 0-4			Score of 5-10		
	No.	%	Total	No.	%	Total	No.	%	Total	No.	%	Total	No.	%	Total	No.	%	Total	No.	%	Total	No.	%	Total
	Regional	1	0.6	166	99.4	166	24	30.8	54	69.2	78	25	25.5	73	74.5	98	43	5.1	794	94.9	837	210	10.4	1,809
General	28	41.8	39	58.2	67	11	21.2	41	78.8	52	88	31.0	196	69.0	284	210	10.4	1,809	89.6	2,019	2,019			
Total	29		204		233	35		95		130	113		269		382	253		2,603			2,856			

* Expected distribution of scores based on previous experience in 1,319 elective cesarean sections: 0-4 18%; 5-10 82%; $\chi^2 = 60.0$; $p < 0.001$.

† Expected distribution of scores on the above 2,856 cases using null hypothesis: 0-4 9.7%; 5-10 90.3%; $\chi^2 = 37.9$; $p < 0.001$.

liveries under general anesthesia was approximately three times greater than under regional ($p < 0.001$). A detailed analysis of the TSR's of all full-term vaginal vertex deliveries is presented in table 6. An arbitrary division was made at 150 seconds, and respiration was considered delayed after this time. Respiration was not well established before two-and-a-half minutes in 7% of this group. Of this 7% more than three out of four had received general anesthesia.

Biochemical Data

The transfer of cyclopropane across the placenta was studied by manometric analysis of simultaneously drawn samples of maternal and umbilical cord blood for content of cyclopropane at the time of delivery. Twenty-five mothers who received only cyclopropane and oxygen for anesthesia during the second stage of labor were studied.

Blood gas analyses were performed on the Kopp-Natelson microgasometer with use of a modification of the method of Holaday and Verosky.⁹ Cyclopropane and dissolved nitrogen were estimated by measurement of the pressure of the residual gas left

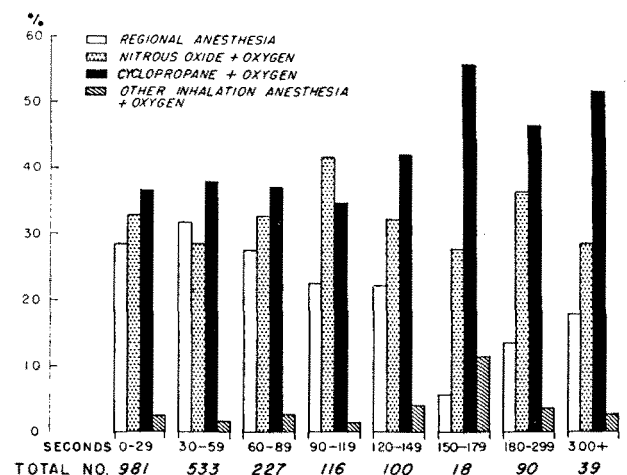


Fig. 3.—Time of sustained respiration in seconds in full-term vaginal vertex presentations.

nitrogen washout from maternal and fetal blood in a group of six mothers breathing 100% oxygen in a nonrebreathing system for periods of 5 to 60 minutes indicated that the nitrogen content of

maternal blood was lowered rapidly during breathing of atmospheres low in nitrogen (table 8 and fig. 5). The nitrogen content of the fetal blood fell slowly and was not significantly altered in 10 minutes of maternal washout. In view of the fact that cyclopropane was usually administered intermittently, with air breathing sometimes allowed between pains, and since the average duration of cyclopropane adminis-

TABLE 5.—Time to Sustained Respiration, in Seconds*

Type of anesthetic.	Breech Deliveries, TSR, Sec.†				Vaginal Vertex Full-term Deliveries, TSR, Sec.‡				Total No.
	0-119		150+		0-119		150+		
	No.	%	No.	%	No.	%	No.	%	
Regional	43	87.8	6	12.2	562	96.6	20	3.4	582
General	126	89.1	15	11.9	1,395	90.9	127	9.1	1,522
Total					1,957		147		2,104

were analyzed using the double scale cuvette oximeter⁹ or the Beckman spectrophotometer.¹⁰ All three methods were standardized against the Van Slyke. The results of analyses for oxygen and carbon dioxide, pH, hematocrit, and buffer-base will be reported elsewhere.¹¹

TABLE 7.—Average Residual Nitrogen Content of Fifteen Blood Samples from Five Mothers and Their Infants

Nitrogen Blood Level, Vol. %			
Maternal Artery	Maternal Vein	Umbilical Vein	Umbilical Artery
0.9
1.4	0.5	1.7	1.3
1.0	0.9	0.8	0.8
0.4	...	1.8	1.4
...	1.4	1.6	1.7

n = 15
mean = 1.2 vol. %, S.D. = ± 0.45 vol. %.

In the experimental group no specific plan of random selection was adopted. Cases were chosen in relation to the availability of the laboratory facilities. However, there were no cases of fetal distress in this group.

Results

The blood of most infants delivered of mothers receiving cyclopropane contained this gas in demonstrable amounts (table 9). The amount of cyclopropane in umbilical cord blood was usually less than, but proportionate to, the amount in maternal extremity vein blood. The few maternal arterial blood samples obtained during this study suggest that the maternal tissues were not in equilibrium with the concentration of cyclopropane in the blood at the time of sampling. The maternal-fetal gradient was probably greater than shown by the comparison of maternal vein blood and umbilical vein blood.

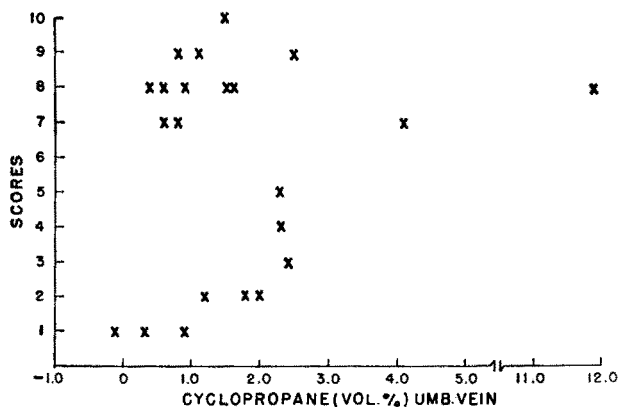


Fig. 6.—Relation of scores to concentration of cyclopropane in umbilical vein.

There was no obvious correlation between the concentration of cyclopropane in the umbilical cord blood and the scores of the infants (fig. 6). Further, no obvious correlation was found between birth oxygenation and score. However, if oxygenation and

score be compared in the regional and cyclopropane groups, the latter appears more depressed for a given level of oxygen saturation (fig. 7).

Comment

The clinical study indicates that infants delivered with the mother under general anesthesia are more depressed than those delivered with the mother under regional anesthesia, although the mortality in the two groups is not different. In addition the

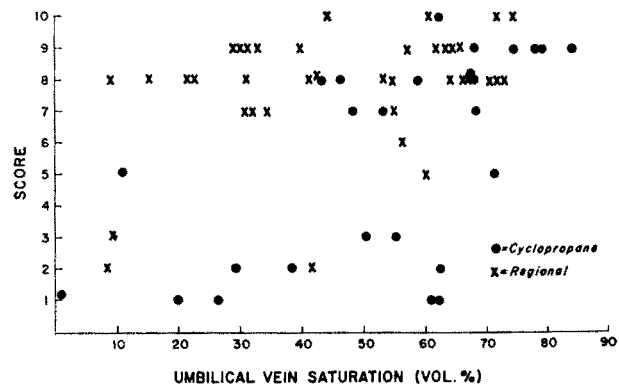


Fig. 7.—Comparison of umbilical vein oxygen saturation and scores.

average depression of infants receiving cyclopropane is significantly greater than is seen when regional or other methods of inhalation anesthesia are used (table 10). If these findings are not due to an inadvertent selection of cases, it remains to be determined whether the gas is exerting a direct narcotic action on the fetus or is depressing the infant by interfering with placental or maternal respiration.

TABLE 8.—Nitrogen Washout from Maternal and Umbilical Cord Blood in Six Mothers, with 100% Oxygen, Nonrebreathing Technique

Time of Oxygen Administration, Min.	Nitrogen Blood Level, Vol. %		
	Maternal Vein	Umbilical Vein	Umbilical Artery
5.....	0.0
32.....	-0.3
30.....	0.7	0.8	0.4
8.....	0.3	1.4	...
22.....	...	1.1	1.8
40*.....	0.1
60.....	-0.4	...	0.0

* Data for same patient as line 4.

The oxygen saturations (table 11) and carbon dioxide tensions¹¹ of umbilical vein blood in both regional and cyclopropane groups were not significantly different. The pH in the cyclopropane group was 0.07 units higher.¹¹ These findings argue against the gas interfering with placental function and favor a direct action on the fetus.

In agreement with Rovenstine's study,³ no correlation between the condition of the infant at birth and the blood level of cyclopropane was demon-

strated. This suggests that some factor other than the anesthetic agent is depressing the infant. However, the blood levels are only of value as an indication of the depth of anesthesia when equilibrium between the blood and tissues has been reached.

TABLE 9.—Cyclopropane Levels in Maternal and Fetal Blood

Type of Delivery	Time Cyclo., Min.*	Mat. Artery, Vol. %†	Mat. Vein, Vol. %‡	Umbilical Vein, Vol. %	Umbilical Artery, Vol. %	Score
Vaginal Vertex	15		1.9	0.6		8
Vaginal Vertex	14		1.6			
Vaginal Vertex	15			0.6		7
Vaginal Vertex	4.5		4.1	2.3		5
Cesarean Section	10.0		6.2			
	10.5			2.4		3
Vaginal Vertex	13.0		2.6	1.6		8
Vaginal Vertex	6.5		2.6			
	7.5			0.9		8
Cesarean Section	7.0			0.3		1
	13.25		2.7			
Vaginal Vertex	2.0		2.2			
	4.0			1.2		2
Vaginal Vertex	1.5		1.5	1.5		8
Vaginal Vertex	5.0			0.4		8
	5.5		1.0			
Vaginal Vertex	13.5		1.4	1.1		9
Vaginal Vertex	9.5		2.8			
	10.0			1.8		2
Vaginal Vertex	?		3.3	1.5		10
Vaginal Vertex	7.0			0.8		7
	10.0		1.6			
Vaginal Vertex	8.5		3.4	2.5		9
Cesarean Section	?	6.2		0.9		1
Vaginal Vertex	10.0	5.3		2.0		2
Vaginal Vertex	3.0		8.5	4.1		7
Cesarean Section	17.0		3.0			
Vaginal Vertex	3.0		1.1	—0.1	0.3	1
Vaginal Vertex	1.5		4.4	0.8		9
Cesarean Section	6.0	3.7				5
	10.0		5.9§			
Vaginal Vertex	6.0	8.2				4
Cesarean Section	?	4.5		2.3	0.5	3
Cesarean Section	6	23.0		11.9	6.5	8
n =		6	20	22		24
mean =		8.5	3.1	1.8		5.6
standard deviation =		±7.5	±1.9	±1.9		±3.3

* Time cyclo. = time in minutes from first inhalation of cyclopropane to moment of sampling.

† Mat. Art. = brachial or radial artery.

‡ Mat. Vein = antecubital vein.

§ Uterine vein sample.

Since equilibrium was not reached in this study due to the brief or intermittent periods of administration, little can be inferred from this lack of correlation.

TABLE 10.—Significance of Difference Between Means

	t	p
Maternal artery: maternal vein	4.74	<0.001
Maternal vein: umbilical vein	3.06	<0.01
Umbilical vein: control		
(mean cyclopropane = 0.0 vol. %; n = 4)	5.5	<0.001
Maternal vein: control		
(mean cyclopropane = 0.0 vol. %; n = 3)	8.8	<0.001
Mean score of infants in cyclopropane group:		
mean score of all infants (7.6 ± 2.3; n = 12,267)	5.4	<0.001

The immediately apparent explanation for the direct action of cyclopropane on the infants is a mild and readily reversible central narcosis. However, the toxic action of this agent on cardiac muscle,¹² especially in the presence of high tensions of carbon dioxide,¹³ is well known. Since in emer-

gency obstetric situations with fetal distress the infant will be both anoxic and hypercarbic, the possibility of some interference with cardiac function should be considered.

Conclusions

In both clinical and biochemical studies infants born with the mother under general anesthesia, and specifically cyclopropane, were more depressed than those born with the mother under regional anesthesia. Cyclopropane is transferred rapidly to the fetus, but as used clinically in this study equilibrium with the mother was not reached. There was no bio-

TABLE 11.—Scores and Umbilical Cord Oxygenation

Type of Anesthesia and Type of Delivery	Av. Score	No.	Umbilical Vein, % Sat-uration No.	Umbilical Artery, % Sat-uration No.	Maternal Artery, % Sat-uration No.	No.
Cyclopropane, vaginal	5.9	22	55	22	5	4
Regional, vaginal	8	14	51	14	21	13
Cyclopropane, section	5.4	5	49.2	5	23	5
Regional, section	7.6	26	46.4	26	16	23

chemical evidence that cyclopropane depressed placental function. This suggests that the gas exerted a direct narcotic action on the fetus, despite the absence of correlation between the blood concentration of the gas and the condition of the infant at birth. Toxic action of cyclopropane in relation to the low oxygen and high carbon dioxide levels normally present at birth is possible.

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